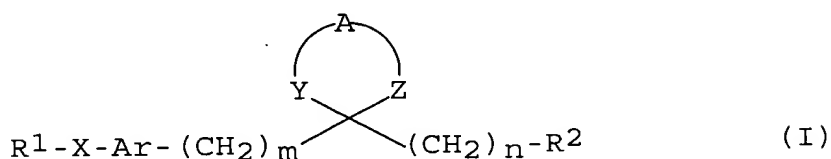


IN THE CLAIMS

The following listing of claims will replace all prior versions, listings, of claims in this application:

Claims 1-17 (Canceled).

Claim 18 (Previously Presented): A compound of the formula:



in which  $\text{R}^1$  is lower alkyl, halogen, optionally substituted heterocyclic group or optionally substituted aryl,

$\text{R}^2$  is carboxy, protected carboxy or amidated carboxy,

Ar is thienyl,

A is ethylene or trimethylene,

X is oxa or a single bond,

Y is thia, sulfinyl or sulfonyl,

Z is methylene,

m and n are each an integer of 0 to 6, and

$$1 \leq m+n \leq 6,$$

and its salt.

Claim 19 (Previously Presented) The compound of claim 18, in which the heterocyclic group of  $\text{R}^1$  is selected from the group consisting of:

- (1) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (2) saturated 3- to 8-membered, heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (3) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 sulfur atoms,
- (4) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 to 5 nitrogen atoms,
- (5) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms,
- (6) saturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms,
- (7) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,
- (8) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 oxygen atoms,
- (9) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 sulfur atoms,
- (10) saturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,
- (11) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,
- (12) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 sulfur atoms and 1 to 3 nitrogen atoms,

(13) saturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 sulfur atoms and 1 to 3 nitrogen atoms, and

(14) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 sulfur atoms and 1 to 3 nitrogen atoms, and

the aryl group of R1 is C6-C10 aryl, and further,

each of the above-mentioned heterocyclic group and aryl group are optionally

substituted by a group selected from the group consisting of:

(A1) halogen,

(A2) lower alkyl,

(A3) lower alkoxy,

(A4) halo(lower)alkyl,

(A5) halo(lower)alkoxy,

(A6) lower alkenyl,

(A7) acyl,

(A8) lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl,

(A9) C6-C10 aryl,

(A10) halo(C6-C10)aryl,

(A11) hydroxy,

(A12) hydroxy(lower)alkyl, protected hydroxy(lower)alkyl,

(A13) amino,

(A14) carboxy,

(A15) protected carboxy,

(A16) nitro(lower)alkenyl,

(A17) lower alkylenedioxy,

(A18) acylamino,

- (A19) nitro,
- (A20) (C6-C10)aryl(lower)alkoxy,
- (A21) carbamoyl(lower)alkenyl optionally N-substituted by the group consisting of lower alkyl, C6-C10 aryl, lower alkoxy(C6-C10)-aryl, and halo(C6-C10)aryl,
- (A22) lower alkylaminocarbonyloxy,
- (A23) lower alkanoyloxy,
- (A24) lower alkoxy(lower)alkanoyloxy,
- (A25) lower alkoxycarbonyloxy,
- (A26) lower alkenoyloxy optionally substituted by heterocyclic group of the above (1) to (14),
- (A27) lower cycloalkanecarbonyloxy,
- (A28) lower alkoxy substituted by the group consisting of carboxy, protected carboxy, lower alkanoyl, lower cycloalkanecarbamoyl, and lower alkylcarbamoyl,
- (A29) lower alkylcarbamoyloxy(lower)alkyl,
- (A30) lower alkoxycarbonylamino(lower)alkyl,
- (A31) amino(lower)alkyl,
- (A32) lower alkylcarbamoyl(lower)alkyl,
- (A33) heterocyclic-carbonylamino, the heterocyclic group being selected from the above (1) to (14) and optionally being substituted N-protective group,
- (A34) the above heterocyclic groups (1) to (14) being optionally substituted by lower alkyl, and
- (A35) oxo.

Claim 20 (Currently Amended): The compound of claim 19, in which

R1 is lower alkyl, halogen, optionally substituted heterocyclic group, or aryl selected from the group consisting of phenyl and naphthyl;

R2 is carboxy, lower alkoxy carbonyl, hydroxyaminocarbonyl, tetrahydropyranyloxyaminocarbonyl, or phenyl(lower)alkylaminocarbonyl, and

m and n are each an integer of 0 or 1, and  $m+n=1$  or 2,

wherein the heterocyclic group is selected from the group consisting of:

- (1) unsaturated 5- or 6-membered heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (2) saturated 5- or 6-membered, heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (3) unsaturated 5- or 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms,
- (4) unsaturated bicyclic 9- or 10-membered, heterocyclic group containing 1 to 5 nitrogen atoms,
- (5) unsaturated 5- or 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms,
- (6) saturated 5- or 6-membered, heteromonocyclic group containing 1 or 2 oxygen atoms,
- (7) unsaturated 5- or 6-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,
- (8) unsaturated bicyclic 9- or 10-membered, heterocyclic group containing 1 or 2 oxygen atoms,
- (9) unsaturated bicyclic 9- or 10-membered, heterocyclic group containing 1 or 2 sulfur atoms, ~~or~~ and

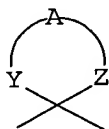
(10) saturated 5- or 6-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,

wherein the heterocyclic group being optionally substituted by a group selected from the group consisting of the following (B1) to (B8):

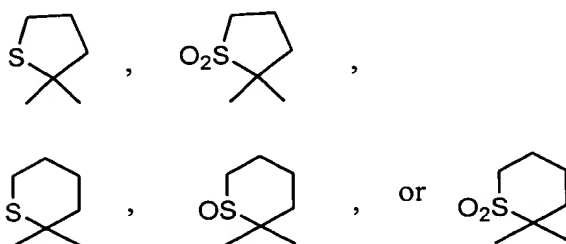
- (B1) lower alkanoyl,
- (B2) lower alkyl,
- (B3) lower alkoxy,
- (B4) lower alkoxycarbonylamino,
- (B5) carbamoyl or lower alkylcarbamoyl,
- (B6) lower alkoxycarbonyl,
- (B7) halo, and
- (B8) oxo;

and the aryl is optionally substituted by a group selected from the group consisting of (A1) to (A35) as defined in claim 19.

Claim 21 (Currently Amended): The compound of claim 20, in which a group of the formula:



is one of the following formulae:



R1 is lower alkyl, halogen, optionally substituted heterocyclic group or aryl selected from the group consisting of phenyl and naphthyl;

R2 is carboxy, lower alkoxycarbonyl, hydroxyaminocarbonyl, or tetrahydropyranyloxyaminocarbonyl, and

m and n are each an integer of 0 or 1, and  $m+n=1$  or 2,

wherein the above-mentioned heterocyclic group is

- (1) pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyridyl N-oxide, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl, tetrazolyl, dihydrotriazinyl,
- (2) azetidiny, pyrrolidinyl, imidazolidinyl, piperidinyl, piperidino, pyrazolidinyl, piperazinyl,
- (3) thienyl,
- (4) indolyl, isoindolyl, indoliziny, benzimidazolyl, quinolyl, isoquinolyl, tetrahydroisoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridyl, tetrazolopyridazinyl, dihydrotriazolopyridazinyl,
- (5) furyl,
- (6) oxolanyl,
- (7) oxazolyl, isoxazolyl, oxadiazolyl,
- (8) benzofuranyl, benzodihydrofuranyl, benzodioxolenyl,
- (9) benzothienyl, dihydrobenzothienyl,
- (10) morpholinyl, or morpholino,

wherein the heterocyclic group being optionally substituted by a group selected from the group consisting of (B1) to (B8) as defined in claim 20,

and the aryl is optionally substituted by a group selected from the group consisting of the following (A1) to (A34):

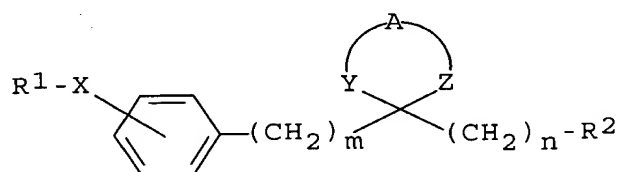
- (A1) halogen,

- (A2) lower alkyl,
- (A3) lower alkoxy,
- (A4) halo(lower)alkyl,
- (A5) halo(lower)alkoxy,
- (A6) lower alkenyl,
- (A7) acyl,
- (A8) lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl,
- (A9) C6-C10 aryl
- (A10) halo(C6-C10)aryl,
- (A11) hydroxy,
- (A12) hydroxy(lower)alkyl or protected hydroxy(lower)alkyl,
- (A13) amino,
- (A14) carboxy,
- (A15) protected carboxy,
- (A16) nitro(lower)alkenyl,
- (A17) lower alkylenedioxy,
- (A18) acylamino,
- (A19) nitro,
- (A20) (C6-C10)aryl(lower)alkoxy,
- (A21) carbamoyl(lower)alkenyl optionally N-substituted by the group consisting of lower alkyl, (C6-C10)aryl, lower alkoxy(C6-C10)-aryl, and halo(C6-C10)aryl,
- (A22) lower alkylaminocarbonyloxy,
- (A23) lower alkanoyloxy,
- (A24) lower alkoxy(lower)alkanoyloxy,
- (A25) lower alkoxycarbonyloxy,

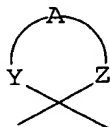


- (A26) lower alkenyloxy optionally substituted by the above heterocyclic group (1),
- (A27) lower cycloalkanecarbonyloxy,
- (A28) lower alkoxy substituted by the group consisting of carboxy, protected carboxy, lower alkanoyl, lower cycloalkanecarbamoyl, and lower alkylcarbamoyl,
- (A29) lower alkylcarbamoxy(lower)alkyl,
- (A30) lower alkoxy-carbonylamino(lower)alkyl,
- (A31) amino(lower)alkyl,
- (A32) lower alkylcarbamoyle(lower)alkyl,
- (A33) heterocyclic-carbonylamino, the heterocyclic group being selected from the above (2), (4) and (5) and optionally substituted by N-protective group, and
- (A34) the heterocyclic group of the above (7) being optionally substituted by lower alkyl.

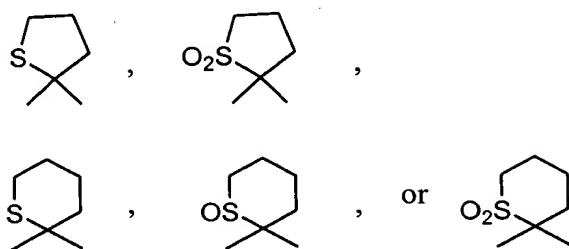
Claim 22 (Previously Presented): The compound of claim 21, having the following formula:



wherein a group of the formula:



is one of the following formulae:



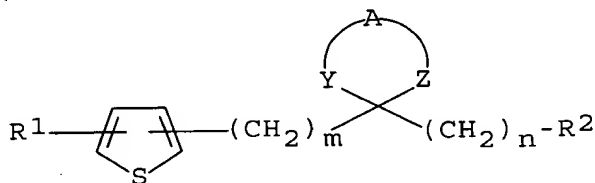
$R^1$  is lower alkyl, phenyl, halophenyl, or (halo)(phenyl)phenyl,

$R^2$  is carboxy or hydroxyaminocarbonyl, and

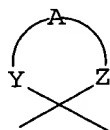
$m$  and  $n$  are each an integer of 0 or 1, and  $m+n=1$ .

Claim 23 (Currently Amended): The compound of claim 21, having the following

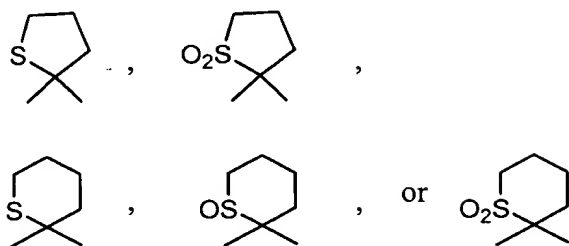
formula:



wherein a group of the formula:



is one of the following formulae:



R<sub>2</sub> is carboxy or hydroxyaminocarbonyl,  
 m and n are each an integer of 0 or 1, and m+n=1,  
 R<sub>1</sub> is halogen, heterocyclic group selected from the group consisting of  
 pyridyl, thienyl, furyl, benzofuranyl or benzothienyl, wherein the heterocyclic group  
 is optionally substituted by a group selected from the group consisting of lower alkanoyl,  
 lower alkyl, lower alkoxy, lower alkoxy-carbonylamino and lower alkylcarbamoyl; naphthyl or  
 phenyl optionally substituted by a group selected from the group consisting of the following  
 (C1) to (C31):

- (C1) halogen,
- (C2) lower alkyl,
- (C3) lower alkoxy,
- (C4) halo(lower)alkyl,
- (C5) halo(lower)alkoxy,
- (C6) lower alkenyl,
- (C7) lower alkylcarbamoyl, carbamoyl, phenyl(lower)alkylcarbamoyl, lower  
 alkanoyl,
- (C8) lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl,
- (C9) phenyl, naphthyl,
- (C10) halophenyl,
- (C11) hydroxy,

- (C12) mono- or dihydroxy(lower)alkyl, phenoxycarbonyloxy(lower)alkyl
- (C13) amino,
- (C14) carboxy,
- (C15) lower alkylenedioxy,
- (C16) lower alkanoylamino,
  - phenyl(lower)alkanoylamino, halophenyl(lower)alkanoylamino,
  - lower alkoxy(lower)alkanoylamino,
  - phenoxy(lower)alkanoylamino, lower alkoxyphenoxy(lower)alkanoylamino,
  - lower alkylphenoxy(lower)alkanoylamino,
  - halophenoxy(lower)alkanoylamino,
  - carboxy(lower)alkanoylamino, lower alkoxycarbonyl(lower)alkanoylamino,
  - lower alkylcarbamoyl(lower)alkanoylamino,
  - halo(lower)alkanoylamino,
  - lower alkenyl(lower)alkanoylamino,
  - lower alkoxy(lower)alkanoylamino,
  - phenyl(lower)alkoxy(lower)alkanoylamino,
  - piperidinyloxy(lower)alkanoylamino, N-lower alkoxycarbonylpiperidinyloxy-(lower)alkanoylamino, pyridyloxy(lower)alkanoylamino,
  - hydroxy(lower)alkanoylamino,
  - lower alkanoyloxy(lower)alkanoylamino,
  - lower alkylcarbamoyloxy(lower)alkanoylamino, N,N-di(lower alkyl)carbamoyloxy,
  - piperidino-carbonyloxy(lower)alkanoylamino,
  - phenyl(lower)alkylcarbamoyloxy(lower)alkanoylamino, lower alkoxycarbonylamino(lower)alkanoylamino,

amino(lower)alkanoylamino, fluorenylmethoxycarbonylamino(lower)-  
alkanoylamino,  
lower alkylamino(lower)alkanoylamino, [N,N-di(lower  
alkyl)amino](lower)alkanoylamino,  
[N-lower alkyl-N-(lower alkoxycarbonyl)-amino](lower)alkanoylamino, [N-  
lower alkyl-N-(fluorenylmethoxycarbonyl)amino](lower)alkanoylamino,  
[N-lower alkyl-N-(mono- or di(lower)-  
alkylcarbamoyl)amino](lower)alkanoylamino,  
[N-(mono- or di(lower alkyl)carbamoyl)amino](lower)alkanoylamino,  
benzoylamino(lower)alkanoylamino, lower  
alkanoylamino(lower)alkanoylamino, lower  
alkanesulfonylamino(lower)alkanoylamino,  
lower alkoxy(lower)alkanoylamino(lower)alkanoylamino,  
cyclo(lower)alkyloxycarbonylamino-(lower)alkanoylamino,  
pyridylcarbonylamino(lower)alkanoylamino,  
morpholinocarbonylamino(lower)alkanoylamino,  
phenyl(lower)alkoxyoxycarbonylamino(lower)alkanoylamino,  
lower alkoxyphenylsulfonylamino(lower)alkanoylamino,  
hydroxy(lower)alkylamino(lower)alkanoylamino,  
morpholino(lower)alkanoylamino, oxooxazolidinyl(lower)alkanoylamino,  
oxopyrrolidinyl(lower)alkanoylamino,  
trimethylhydantoinyl(lower)alkanoylamino,  
lower alkenylamino(lower)alkanoylamino,  
lower alkoxy(lower)alkylamino(lower)alkanoylamino,  
phenyl(lower)alkylamino(lower)alkanoylamino,

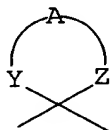
pyridyl(lower)alkylamino(lower)alkanoylamino,  
lower alkoxy carbonylamino, phenyl(lower)alkoxy carbonylamino,  
lower alkoxy(lower)alkoxy carbonylamino,  
halo(lower)alkoxy carbonylamino,  
amino(lower)alkoxy carbonylamino, phthalimido(lower)alkoxy carbonylamino,  
carbamoylamino,  
(mono- or di(lower alkyl)carbamoylamino,  
naphthylcarbamoylamino,  
halophenylcarbamoylamino,  
lower alkoxyphenylcarbamoylamino,  
lower alkenylcarbamoylamino,  
cyclo(lower)alkyl(lower)alkylcarbamoylamino,  
phenyl(lower)alkylcarbamoylamino,  
halo(lower)alkylcarbamoylamino,  
lower alkoxy(lower)alkylcarbamoylamino,  
hydroxy(lower)alkylcarbamoylamino, (lower  
alkyl)(diphenyl)silyloxy(lower)alkylcarbamoylamino,  
carboxy(lower)alkylcarbamoylamino, lower  
alkoxy carbonyl(lower)alkylcarbamoylamino,  
lower alkylcarbamoyl(lower)alkylcarbamoylamino, or  
pyridylcarbamoylamino,  
lower alkylsulfonylamino,  
lower alkenoylamino,  
lower cycloalkanecarbonylamino,  
lower alkenyloxy carbonylamino,

- phenoxycarbonylamino,
- lower alkylthiocarbonylamino,
- (C17) phenyl(lower)alkoxy,
- (C18) lower alkenyl, mono- or di(lower alkyl)carbamoyl(lower)alkenyl, (2-(methylcarbamoyl)ethenyl, 2-(ethylcarbamoyl)ethenyl, 2-(propylcarbamoyl)ethenyl, 2-(isopropylcarbamoyl)ethenyl, 2-(dimethylcarbamoyl)ethenyl,)
- phenylcarbamoyl(lower)alkenyl,
- lower alkoxycarbamoyl(lower)alkenyl,
- halophenylcarbamoyl(lower)alkenyl,
- (C19) lower alkylaminocarbonyloxy,
- (C20) lower alkanoyloxy,
- (C21) lower alkoxy(lower)alkanoyloxy,
- (C22) lower alkoxycarbonyloxy,
- (C23) pyridyl(lower)alkenoyloxy
- (C24) lower cycloalkanecarbonyloxy,
- (C25) carboxy(lower)alkoxy,
- lower alkoxycarbonyl(lower)alkoxy,
- lower alkanoyl(lower)alkoxy,
- lower cycloalkanecarbamoyl(lower)alkoxy,
- lower alkylcarbamoyl(lower)alkoxy,
- (C26) lower alkylcarbamoyloxy(lower)alkyl,
- (C27) lower alkoxycarbonylamino(lower)alkyl,
- (C28) amino(lower)alkyl,
- (C29) lower alkylcarbamoyl(lower)alkyl,

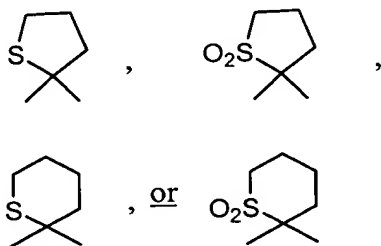
(C30) furylcarbonylamino, teretahydroisoquinolylcarbonylamino, N-lower  
 alkoxy carbonyl-teretahydroisoquinolylcarbonylamino,  
 pyrrolidinylcarbonylamino, and

(C31) oxazolyl, lower alkyloxadiazolyl.

Claim 24 (Currently Amended): The compound of claim 23, in which a group of the  
 formula:



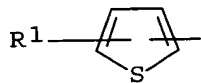
is one of the following formulae:



$R^2$  is hydroxyaminocarbonyl,

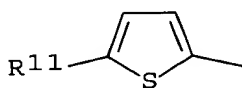
m is 0 and n is 1,

a group of the formula:



is a group selected from the group of the following formulae (a) to (e);

(a)



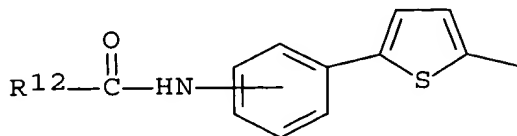
wherein



R<sup>11</sup> is halo, naphthyl, phenyl, mono- or dihalophenyl, mono- or di(lower)alkylphenyl, lower alkoxyphenyl, trihalo(lower)alkylphenyl, trihalo(lower)alkoxyphenyl, lower alkenylphenyl, lower alkylcarbamoylphenyl, carbamoylphenyl, phenyl(lower)alkylcarbamoylphenyl, lower alkanoylphenyl, lower alkylthiophenyl, lower alkylsulfinylphenyl, lower alkylsulfonylphenyl, phenylphenyl, (halo)(phenyl)phenyl, halophenylphenyl, hydroxyphenyl, mono- or dihydroxy(lower)alkylphenyl, phenoxycarbonyloxy(lower)alkylphenyl, aminophenyl, carboxyphenyl, lower alkylendioxyphenyl, lower alkanesulfonylaminophenyl, lower alkenoylaminophenyl, lower cycloalkanecarbonylaminophenyl, phenyl(lower)alkoxyphenyl, mono- or di(lower alkyl)carbamoyl(lower)alkenylphenyl, phenylcarbamoyl(lower)alkenylphenyl, lower alkoxy-carbamoyl(lower)alkenylphenyl, halophenylcarbamoyl(lower)alkenylphenyl, lower alkylcarbamoyloxyphenyl, lower alkanoyloxyphenyl, lower alkoxy(lower)alkanoyloxyphenyl, lower alkoxy-carbonyloxyphenyl, pyridyl(lower)alkenoyloxyphenyl, cyclo(lower)alkylcarbonyloxyphenyl, carboxy(lower)alkoxyphenyl, lower alkoxy-carbonyl(lower)alkoxyphenyl, lower alkanoyl(lower)alkoxyphenyl, lower cycloalkanecarbamoyl(lower)alkoxyphenyl, lower alkylcarbamoyl(lower)alkoxyphenyl, lower alkylcarbamoyloxy(lower)alkylphenyl, lower alkoxy-carbonylamino(lower)alkylphenyl, amino(lower)alkylphenyl, lower alkylcarbamoyl(lower)alkylphenyl, furylcarbonylaminophenyl, 1,2,3,4-teretahydroisoquinolylcarbonylaminophenyl, N-t-butoxycarbonyl 1,2,3,4-teretahydroisoquinolylcarbonylaminophenyl,

pyrrolidinylcarbonylaminophenyl, oxazolylphenyl, or lower  
alkyloxadiazolylphenyl.

(b)

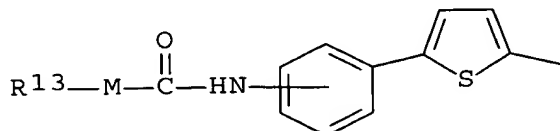


wherein

$R^{12}$  is lower alkyl optionally substituted by a substituents selected from the group  
consisting of phenyl, halophenyl, lower alkoxyphenyl, lower alkoxy, phenoxy,  
lower alkoxyphenoxy, halophenoxy, lower alkylphenoxy, carboxy, lower  
alkoxycarbonyl, lower alkylcarbamoyl, halo, lower alkenyloxy, lower  
alkoxy(lower)alkoxy, phenyl(lower)alkoxy, piperidinyloxy, N-lower  
alkoxycarbonyl-piperidinyloxy, pyridyloxy, hydroxy, lower alkanoyloxy,  
mono- or di(lower)alkylcarbamoxyloxy, piperidinylcarbonyloxy,  
phenyl(lower)alkylcarbamoxyloxy, lower alkoxycarbonylamino, amino,  
fluorenylmethoxycarbonylamino, mono- or di(lower)alkylamino, N-lower  
alkyl-N-(lower alkoxycarbonyl)amino, N-lower  
alkyl-N-(fluorenylmethoxycarbonyl)amino, N-lower alkyl-N-(mono- or  
di(lower)alkylcarbamoyl)amino, N-(mono- or di(lower  
alkyl)carbamoyl)amino, benzoylamino, lower alkanoylamino, lower  
alkanesulfonylamino, lower alkoxy(lower)alkanoylamino,  
cyclo(lower)alkyloxycarbonylamino, pyridylcarbonylamino,  
morpholinocarbonylamino, phenyl(lower)alkoxycarbonylamino, lower

alkoxyphenylsulfonylamino,  
 hydroxy(lower)alkylamino, morpholino,  
 oxooxazolidinyl, oxopyrrolidinyl, trimethylhydantoinyl, pyridyl, lower  
 alkenylamino, lower alkoxy(lower)alkylamino, phenyl(lower)alkylamino,  
 pyridyl(lower)alkylamino, and cyclo(lower)alkyl,

(c)



wherein

M is oxygen or sulfur,

$R^{13}$  is lower alkyl, phenyl(lower)alkyl,

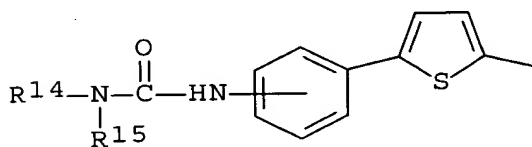
lower alkoxy(lower)alkyl, halo(lower)alkyl,

amino(lower)alkyl, or

phthalimido(lower)alkoxycarbonylamino,

lower alkenyl, or phenyl,

(d)



wherein

$R^{15}$  is hydrogen or lower alkyl,

$R^{14}$  is hydrogen, lower alkyl, naphthyl, halophenyl, lower alkoxyphenyl, lower

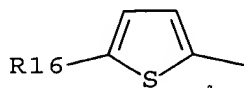
alkenyl, lower cycloalkyl(lower)alkyl, phenyl(lower)alkyl, halo(lower)alkyl,

lower alkoxy(lower)alkyl, hydroxy(lower)alkyl, (lower

alkyl)(diphenyl)silyloxy(lower)alkyl, carboxy(lower)alkyl, lower

alkoxycarbonyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl, or ~~pyridyl~~,  
pyridyl; and

(e)

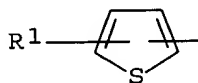


wherein

R16 is benzothienyl, benzofuranyl, thienyl, furyl, lower alkylpyridyl, pyridyl, lower  
 alkoxypyridyl, lower alkoxycarbonylaminopyridyl, lower alkanoylthienyl, or  
 lower alkylcarbamoylbenzofuranyl.

Claim 25 (Currently Amended): The compound of claim 24, wherein

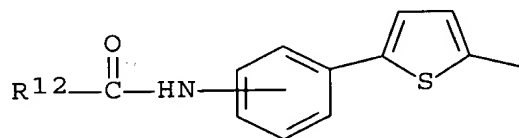
a group of the formula:



is the same group as (a), (c), (d) ~~and~~ or (e) of claim 24, ~~and~~ or the following formula

(b):

(b)



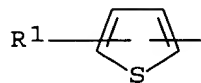
wherein

R<sup>12</sup> is lower alkyl, phenyl(lower)alkyl, halophenyl(lower)alkyl,  
 lower alkoxyphenyl(lower)alkyl,  
 lower alkoxy(lower)alkyl, phenoxy(lower)alkyl, lower  
 alkoxyphenoxy(lower)alkyl, halophenoxy(lower)alkyl,  
 lower alkylphenoxy(lower)alkyl, carboxy(lower)alkyl,  
 lower alkoxycarbonyl(lower)alkyl,

lower alkylcarbamoyl(lower)alkyl, halo(lower)alkyl, lower  
alkenyloxy(lower)alkyl, lower  
alkoxy(lower)alkoxy(lower)alkyl,  
phenyl(lower)alkoxy(lower)alkyl, piperidinyloxy(lower)alkyl,  
N-t-butoxycarbonylpiperidinyloxy(lower)alkyl, pyridyloxy(lower)alkyl,  
hydroxy(lower)alkyl,  
lower alkanoyloxy(lower)alkyl,  
mono- or di(lower)alkylcarbamoyloxy(lower)alkyl,  
piperidinylcarbonyloxy(lower)alkyl,  
phenyl(lower)alkylcarbamoyloxy(lower)alkyl,  
amino(lower)alkyl,  
lower alkoxycarbonylamino(lower)alkyl,  
fluorenylmethoxycarbonylamino(lower)alkyl,  
mono- or di(lower)alkylamino(lower)alkyl,  
N-lower alkyl-N-(lower alkoxycarbonyl)amino(lower)alkyl,  
N-lower alkyl-N-(fluorenylmethoxycarbonyl)amino-  
(lower)alkyl, N-lower alkyl-N-(mono- or di(lower)-  
alkylcarbamoyl)amino(lower)alkyl, N-(mono- or di(lower)alkyl)carbamoyl-  
amino(lower)alkyl, benzoylamino(lower)alkyl,  
lower alkanoylamino(lower)alkyl,  
lower alkanesulfonylamino(lower)alkyl,  
lower alkoxy(lower)alkanoylamino(lower)alkyl,  
cyclo(lower)alkyloxycarbonylamino(lower)alkyl,  
pyridylcarbonylamino(lower)alkyl, morpholinocarbonylamino(lower)alkyl,  
phenyl(lower)alkoxyoxycarbonylamino(lower)alkyl,

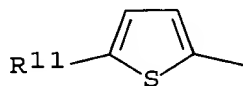
lower alkoxyphenylsulfonylamino(lower)alkyl,  
hydroxy(lower)alkylamino(lower)alkyl, morpholino(lower)alkyl,  
oxooxazolidinyl(lower)alkyl, oxopyrrolidinyl(lower)alkyl,  
trimethylhydantoinyl(lower)alkyl, pyridyl(lower)alkyl, lower  
alkenylamino(lower)alkyl, lower alkoxy(lower)alkylamino(lower)alkyl,  
phenyl(lower)alkylamino(lower)alkyl, pyridyl(lower)alkylamino(lower)alkyl,  
cyclo(lower)alkyl, (amino)(phenyl)(lower)alkylamino, (lower  
alkoxycarbonylamino)(phenyl)(lower)alkyl, (amino)(lower alkoxy)-  
(lower)alkyl, (lower alkoxycarbonylamino)(lower alkoxy)(lower)alkyl,  
(amino)(carboxy)(lower)alkyl, (lower alkoxycarbonylamino)(carboxy)-  
(lower)alkyl, (amino)(lower alkoxycarbonyl)(lower)alkyl, (lower  
alkoxycarbonylamino)(lower alkoxycarbonyl)(lower)alkyl,  
(amino)(phenyl(lower)alkoxy)(lower)alkyl, (lower alkoxycarbonylamino)-  
(phenyl(lower)alkoxy)(lower)alkyl, (amino)(pyridyl)(lower)alkyl,  
(lower alkoxycarbonylamino)(pyridyl)(lower)alkyl, (amino)(hydroxy)-  
(lower)alkyl, (lower alkoxycarbonylamino)(hydroxy)(lower)alkyl,  
(amino)(amino)(lower)alkyl,  
(lower alkoxycarbonylamino)(amino)(lower)alkyl, (amino)(lower  
alkoxycarbonylamino)(lower)alkyl, (lower alkoxycarbonylamino)(lower  
alkoxycarbonylamino)(lower)alkyl,  
(amino)(lower cycloalkane)(lower)alkyl, or  
(lower alkoxycarbonylamino)(lower cycloalkane)(lower)alkyl.

Claim 26 (Currently Amended): The compound of claim 24, in which a group of the  
formula:



is a group selected from the group of the following formula (a) to (e):

(a)



wherein

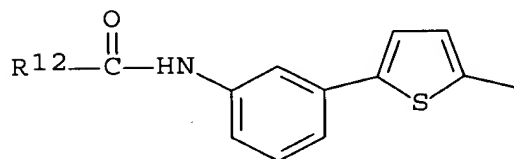
R<sup>11</sup> is bromo, 2-naphthyl, phenyl,  
3(or 4)-chlorophenyl, 2(or 3 or 4)-fluorophenyl,  
3,4-dichlorophenyl, 3,5-difluorophenyl, 3(or 4)-methylphenyl, 4-ethylphenyl,  
4-isopropylphenyl, 4-(t-butyl)phenyl,  
3,4-dimethylphenyl, 4-methoxyphenyl,  
4-ethoxyphenyl, 4-trifluoromethylphenyl,  
4-trifluoromethoxyphenyl, 4-ethenylphenyl,  
4-methylcarbamoylphenyl, 4-ethylcarbamoylphenyl,  
4-carbamoylphenyl, 4-benzylcarbamoylphenyl,  
4-acetylphenyl, 4-methylthiophenyl,  
4-ethylthiophenyl, 4-methylsulfinylphenyl,  
4-methylsulfonylphenyl, phenylphenyl, 4-phenyl-3-fluorophenyl,  
4-(4-fluorophenyl)phenyl, 3(or 4)-hydroxyphenyl, 3(or  
4)-hydroxymethylphenyl,  
4-(1,2-dihydroxyethyl)phenyl,  
4-(phenoxycarbonyloxymethyl)phenyl, 3(or 4)-aminophenyl,  
4-carboxyphenyl,  
3,4-methylenedioxyphenyl,

4-(methanesulfonylamino)phenyl,  
3-(2-butenoylamino)phenyl,  
3-(cyclopropanecarbonylamino)phenyl,  
3-(cyclobutanecarbonylamino)phenyl,  
3-(cyclopentanecarbonylamino)phenyl,  
4-benzyloxyphenyl,  
4-(2-(methylcarbamoyl)ethenyl)phenyl,  
4-(2-(ethylcarbamoyl)ethenyl)phenyl,  
4-(2-(propylcarbamoyl)ethenyl)phenyl,  
4-(2-(isopropylcarbamoyl)ethenyl)phenyl,  
4-2-(dimethylcarbamoyl)ethenyl)phenyl,  
4-(2-(phenylcarbamoyl)ethenyl)phenyl,  
4-(2-(methoxyphenylcarbamoyl)ethenyl)phenyl,  
4-(2-(4-fluorophenylcarbamoyl)ethenyl)phenyl,  
4-(methylaminocarbonyloxy)phenyl,  
4-(ethylaminocarbonyloxy)phenyl,  
4-propanoyloxyphenyl, 4-(methoxyacetyloxy)phenyl, 4-(ethoxycarbonyloxy)phenyl,  
4-(3-(3-pyridyl)acryloyloxy)phenyl,  
4-(cyclopropylcarbonyloxy)phenyl,  
4-(carboxymethoxy)phenyl,  
4-(ethoxycarbonylmethoxy)phenyl,  
4-(t-butoxycarbonylmethoxy)phenyl,  
4-(propanoylmethoxy)phenyl,  
4-(cyclopropylcarbamoylmethoxy)phenyl,



3(or 4)-(methylcarbamoylmethoxy)phenyl,  
 4-(ethylcarbamoylmethoxy)phenyl,  
 4-(propylcarbamoylmethoxy)phenyl,  
 3(or 4)-(methylcarbamoyloxymethyl)phenyl,  
 4-(methoxycarbonylaminomethyl)phenyl,  
 4-(t-butoxycarbonylaminomethyl)phenyl,  
 4-aminomethylphenyl,  
 4-(methylcarbamoylmethyl)phenyl,  
 3-(2(or 3)-furylcarbonylamino)phenyl,  
 3-(1,2,3,4-teretahydroisoquinolylcarbonylamino)phenyl,  
 3-(N-(t-butoxycarbonyl)-1,2,3,4-  
 teretahydroisoquinolylcarbonylamino)phenyl,  
 3-(pyrrolidinylcarbonylamino)phenyl,  
 4-(1,3-oxazolyl)phenyl, or  
 4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl,

(b)



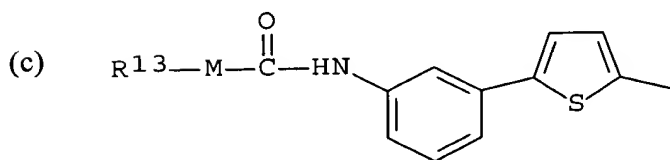
wherein

R<sup>12</sup> is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, neopentyl,  
 phenylmethyl,  
 4-chlorophenylmethyl, 4-methoxyphenylmethyl,  
 methoxymethyl, ethoxymethyl, propoxymethyl, butoxymethyl,

isopropyloxymethyl, 1-methoxyethyl, 2-methoxyethyl,  
phenoxymethyl, 2-phenoxyethyl, 3(or 4)-methoxyphenoxymethyl,  
4-fluoro(or chloro)phenoxymethyl, 3(or 4)-methylphenoxymethyl,  
2-carboxyethyl, 2-methoxycarbonylethyl, 2-t-butoxycarbonylethyl,  
2-methylcarbamoylethyl,  
2-chloroethyl, chloromethyl, allyloxymethyl,  
(2-ethoxyethoxy)methyl, benzyloxymethyl,  
4-piperidinyloxymethyl, (N-t-butoxycarbonyl-4-piperidinyloxy)methyl,  
3(or4)-pyridyloxymethyl, hydroxymethyl, 2-hydroxyethyl,  
acetoxymethyl,  
1-acetoxyethyl, methylcarbamoyloxymethyl, 1-(N-methyl-N-  
ethylcarbamoyloxy)methyl, (piperidino-carbonyloxy)methyl,  
(benzylcarbamoyloxy)methyl,  
(t-butoxycarbonylamino)methyl, aminomethyl,  
1-aminoethyl, 1-(t-butoxycarbonylamino)ethyl,  
2-aminoethyl, methoxycarbonylaminomethyl,  
2-(methoxycarbonylamino)ethyl, ethoxycarbonylaminomethyl,  
propoxycarbonylaminomethyl,  
1-(fluorenylmethoxycarbonylamino)methyl,  
2-(t-butoxycarbonylamino)ethyl,  
2-(fluorenylmethoxycarbonylamino)ethyl,  
1-aminoisopropyl, 1-aminopropyl,  
1-(t-butoxycarbonylamino)propyl,  
1-(t-butoxycarbonylamino)isopropyl,  
1,5-diaminopentyl, 1,5-bis(t-butoxycarbonylamino)-pentyl,

methylaminomethyl, ethylaminomethyl,  
(N-methyl-N-ethylamino)methyl,  
dimethylaminomethyl, pentylaminomethyl,  
t-butylaminomethyl, methylaminoethyl,  
3-(2-(N-methyl-N-methoxycarbonylamino)methyl,  
1-(N-methyl-N-t-butoxycarbonylamino)methyl,  
1-(N-ethyl-N-t-butoxycarbonylamino)methyl,  
2-(N-methyl-N-(fluorenylmethoxycarbonyl)amino)-ethyl,  
2-(N-methyl-N-(t-butoxycarbonyl)amino)ethyl, 1-(N-methyl-N-  
(dimethylcarbamoyl)amino)methyl,  
1-(dimethylcarbamoylamino)methyl,  
1-(N-(ethylcarbamoyl)amino)methyl,  
2-(N-(ethylcarbamoyl)amino)ethyl, benzoylaminomethyl, 2-  
benzoylaminoethyl, acetylaminomethyl, isobutyrylaminomethyl,  
pivaloylaminomethyl,  
1-(methanesulfonylamino)methyl,  
2-(methanesulfonylamino)ethyl, methoxyacetylaminomethyl,  
cyclopentyloxycarbonylaminomethyl,  
pyridylcarbonylaminomethyl, morpholinocarbonylaminomethyl,  
benzyloxycarbonylaminomethyl,  
1-(4-methoxyphenylsulfonylamino)methyl,  
1-(2-hydroxyethylamino)methyl,  
morpholinomethyl, 1-(2-oxo-1,3-oxazolidin-1-yl)methyl,  
1-(2-oxopyrrolidin-1-yl)methyl,  
1-(3,4,4-trimethylhydantoin-1-yl)methyl, allylaminomethyl, 1-(2-

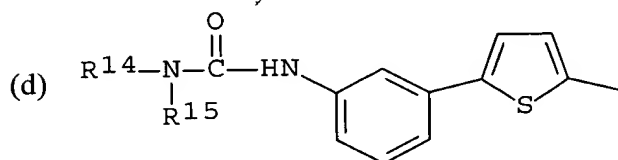
ethoxyethylamino)methyl,  
 benzylaminomethyl, 1-(3-pyridylmethylamino)methyl,  
 2-phenyl-1-aminoethyl, 1-amino-1-phenylmethyl,  
 1-t-butoxycarbonylamino-1-phenylmethyl,  
 1-amino-2-phenylethyl, 1-t-butoxycarbonylamino-2-phenylethyl,  
 1-amino-2-methoxyethyl,  
 1-t-butoxycarbonylamino-2-methoxyethyl, 1-amino-3-carboxypropyl,  
 1-t-butoxycarbonylamino-3-carboxypropyl,  
 1-amino-3-(t-butoxycarbonyl)propyl,  
 1-t-butoxycarbonylamino-3-t-butoxycarbonylpropyl, ~~etc.~~, 1-amino-2-  
 benzyloxyethyl,  
 1-t-butoxycarbonylamino-2-benzyloxyaminoethyl,  
 1-amino-2-(3-pyridyl)ethyl,  
 1-t-butoxycarbonylamino-2-(3-pyridyl)ethyl, 1-  
 amino-2-(4-pyridyl)ethyl,  
 1-t-butoxycarbonylamino-2-(4-pyridyl)ethyl,  
 1-amino-2-hydroxyethyl,  
 1-t-butoxycarbonylamino-2-hydroxyethyl,  
 (1,5-diaminopentyl, 1-t-butoxycarbonylamino-5-aminopentyl,  
 1,5-bis(t-butoxycarbonylamino)pentyl,  
 1-amino-5-(t-butoxycarbonylamino)pentyl, 1-  
 amino-2-cyclohexylethyl, or  
 1-t-butoxycarbonylamino-2-cyclohexylethyl,



wherein

M=O and R13 is methyl, ethyl, propyl, isopropyl, benzyl, 2-methoxyethyl, 2-chloroethyl, 2-aminoethyl, 2-phthalimidoethyl, allyl, ~~phenyl, or~~ phenyl; or

M=S and R13 is methyl or ethyl ~~methyl, ethyl,~~

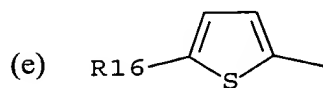


wherein

R15 is hydrogen and

R14 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, hexyl, 1-naphthyl, 3(or 4)-chlorophenyl, 3-methoxyphenyl, allyl, cyclohexylmethyl, benzyl, 2-chloroethyl, methoxymethyl, 2-methoxyethyl, 2-hydroxyethyl, 2-((t-butyl)(diphenyl)silyloxy)ethyl, carboxymethyl, ethoxycarbonylmethyl, methylcarbamoylmethyl, or 3-pyridyl,

R14 is ethyl and R15 is methyl, and



wherein

R16 is 2-benzothieryl, 2-benzofuranyl, 2(or 3)-thienyl, 2-furyl, 3-pyridyl, 1-methyl-4-pyridyl, 6-methyl-3-pyridyl,

6-methoxy-3-pyridyl, 5-methoxycarbonylamino-3-pyridyl, 5-acetyl-2-thienyl, or  
2-methylcarbamoyl-5-benzofuranyl.

Claim 27 (Previously Presented): A pharmaceutical composition which comprises the compound of Claim 18 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or excipient.

Claim 28 (Previously Presented): A process for preparing a pharmaceutical composition which comprises admixing the compound of Claim 18 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable carrier or excipient.

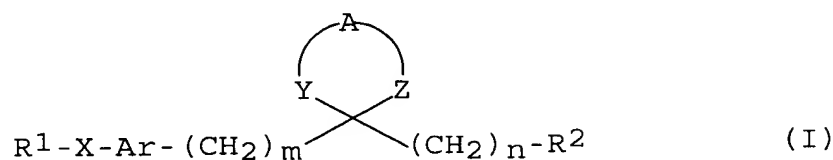
Claim 29 (Currently Amended): A method for treating, ~~reducing, arresting, or~~  
~~alleviating~~ matrix metalloproteinases (MMP) or tumor necrosis factor  $\alpha$  (TNF  $\alpha$ )-mediated disease, the method comprising administering to a patient in need thereof, a therapeutically effective amount of the compound of Claim 18 or a pharmaceutically acceptable salt thereof, wherein the matrix metalloproteinases (MMP) or tumor necrosis factor  $\alpha$  (TNF  $\alpha$ )-mediated disease is selected from the group consisting of arthritis, cerebral disease, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, tumor metastasis, tumor invasion, HIV-infection, autoimmune disease, and sepsis.

Claim 30 (Cancelled).

Claim 31 (Currently Amended): A process for manufacturing ~~a medicament~~the pharmaceutical composition of Claim 27, ~~said process comprising contacting~~ mixing the compound ~~of Claim 18~~ or a pharmaceutically acceptable salt thereof with a the pharmaceutically acceptable carrier.

Claims 32-35 (canceled).

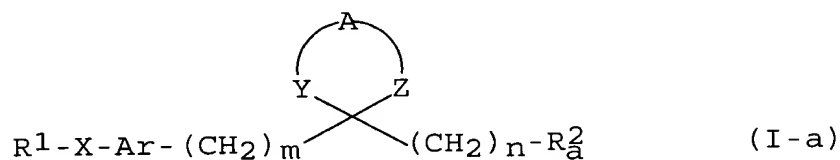
36. (New): A process for the preparation of a compound of the formula:



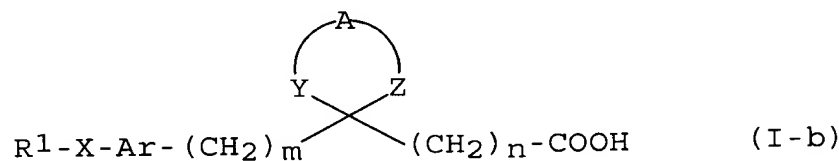
in which  $\text{R}^1$ ,  $\text{R}^2$ , Ar, A, X, Y, Z, m and n are each as defined in Claim 18,

which comprises

(1) subjecting a compound of the formula:



or a salt thereof to removal reaction of the carboxy-protective group, to give a compound of the formula:



or a salt thereof.

37. (New) The method of Claim 39, wherein the matrix metalloproteinases (MMP) or tumor necrosis factor  $\alpha$  (TNF  $\alpha$ )-mediated disease is arthritis.